



#7

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Nucleotide sequence of the entire envelope gene for the mutant HBsAg strain:

ATGGGGCAGAATCTTTCCACCAGCAATCCTCTGGGATTCTTTCCCGACCACCGATTGGAT  
CCAGCCTTCAGAGCAAACACCAACAATCCAGATTGGGACTTCAATCCCAACAAGGACAC  
CTGGCCAGACGCCAACAAGGTAGGAGCTGGAGCATTGGGACTGGGGTTCACCCACCACG  
ACGGAGGCCTTTTGGGGTGGAGCCCTCAGGCTCAGGGCATAACACAAACCTTGCCAGCA  
AATCCGCCTCTGCTTCCACCAATCGCCAGTCAGGAAGGCAGCCTACCCCGCTGTCTCCA  
CCTTTGAGAAACACTCATCTCAAGCCATGCAGTGGAACCTCCACAACCTTCCACCAAAC  
CTGCAAGATCCCAGAGTGAGAGGTCTGTATTTCCCTGCTGGTGGCTCCAGTTCAGGAACAG  
TAAACCTGTTCGACTACTGTCTCTCCCATATCGTCAATCTTCTCGAGGATTGGGGACC  
CTGCGCGGAACATGGAGAACATCACATCAGGATTCTAGGACCCCTGCTCGTGTTACAG  
GCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCGCAGAGCTAGACTCGTGGTG  
GACTTCTCTCAATTTTCTAGGGGGAACCTACCGTGTGTCTTGCCAAAATTCGAGTCCC  
CAACCTCCAATCACTCACCAACCTCTGTCTCCAATGTCTCGTGTATCGCTGGATGT  
GTCTGCGGGCTTTTATCATCTTCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTGGT  
TCTTCTGGACTATCAAGGTATGTTGCCCGTTTGTCTCTAATTCCAGGATCTTCAACCAC  
CAGCAGGGGACCATGCAGAGCCTGCACGACTCCTGCTCAAGGAACCTCTATGTATCCCT  
CCTGTTGCTGTACAAAACCTTCGGATGGAACTGCACCTGTATTCCCATCCCATCATCCT  
GGGCTTTCGGAATACTCTATGGGAGTGGGCCTCAGCCCGTTTCTCCTGGCTCAGTTTAC  
TAGTGCCATTGTTCAGTGGTTCGTAGGGCTTTCCCCACTGTTTGGCTTTCAGTTATATG  
GATGATGTTGTACTGGGGCCAAGTCTGTACCATCTTGAGTCCCTTTTTACCCTGTT  
ACCAATTTCTTTTGTCTTTGGGTATACATTTAAACCTAATAAA

FIG. 1

09821877.09401

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Amino acid sequence of the entire envelope gene for the mutant HBV strain:

[preS1]MGQNLTSTNPLGFFPDHQLDPAFRANTNNPDWDFNPNKDTWPDANKVGAGAFGL  
GFTPHGGLLGWSPQAQGITQTLPANPPPASTNRQSGRQPTLSPPLRNTHPQA

[preS2]MQWNSTTFHQLDQPRVRGLYFAGGSSSGTVNVPVPTTVSPISSIFSRIGDPARN

[S]M<sub>1</sub>ENITSGFLG<sub>10</sub>PLLVLQAGFF<sub>20</sub>LLTRILTIQ<sub>30</sub>SLDSWWTSLN<sub>40</sub>FLGGTTVCLG<sub>50</sub>QNSQS  
PTSNH<sub>60</sub>SPTSCPPTCP<sub>70</sub>GYRMMCLRRF<sub>80</sub>IIFLILLIC<sub>90</sub>LIFLLVLDY<sub>100</sub>QGMLPVCPLI<sub>110</sub>PGS  
STTSTGP<sub>120</sub>CRAC<sub>121</sub>TTPAQG<sub>130</sub>TSMYPSCCCT<sub>140</sub>KPSDGNCTCI<sub>150</sub>PIPSSWAFGK<sub>160</sub>FLWEWASA  
RF<sub>170</sub>SWLSLLVPFV<sub>180</sub>QWFVGLSPTV<sub>190</sub>WLSVIMMMLY<sub>200</sub>WGPSLYTILS<sub>210</sub>PFLPLLPIFF<sub>220</sub>CL  
WVYI.

subtype ayw2, genotype D

Three S substitutions found:

- 1.) Thr to Ala 123 (affects H166 epitope)
- 2.) Trp to Leu 199 (outside "a" determinant)
- 3.) Ser to Thr 207 (outside "a" determinant)

FIG.2

09821877.092401

Nucleotide sequence of the small envelope gene for wild type HBV ayw<sub>2</sub>:

ATGGAGAACATCACATCAGGATTCTAGGACCCCTGCTCGTTACAGCGGGGTTTT  
TCTGGTTGACAAGAATCCTCACAATACCGAGAGTCTAGACTCGTGGTGGACTTCTCTC  
AATTTTCTAGGGGGAACCTACCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCTCCAA  
TCACTCACCAACCTCCTGTCTCCAAC TTGTCTGGTTATCGCTGGATGTGTCTGCGGC  
GTTTTATCATCTTCTCTTCATCCTGCTGCTATGCCCTCATCTTCTTGTGGTTCTTCTGGA  
CTATCAAGGTATGTTGCCGTTTGTCTCTAATTCAGGATCATCAACCACCAGCACGG  
GACCTGCGAGAACCTGCACGACTCCTGCTCAAGGAACCTCTATGTATCCCTCCTGTTGC  
TGTACAAAACCTTCGGATGGAACTGCACCTGTATTCCCATCCCATCATCTGGGCTTT  
CGGAAAATTCCTATGGGAGTGGGCTCAGCCCGTTTCTCTTGGCTCAGTTTACTAGTGC  
CATTTGTTCA GTGGTTCGTAGGGCTTTCCCCACTGTTTGGCTTTCAGTTATATGGATGA  
TGTGGTATTGGGGGCCAAGTCTGTACAGCATCTTGAGTCCCTTTTACCGCTGTTACCA  
ATTTTCTTTTGTCTTTGGGTATACATTTAA

FIG.3

Translated nucleotide sequence of the small envelope gene for the mutant HBV strain (1st sequence) and for wild type ayw<sub>2</sub> (third sequence). Differences in sequence are underlined.

S sequence-->

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GCG CGG AAC ATG GAG AAC ATC ACA TCA GGA TTC CTA GGA CCC CTG CTC GTG TTA CAG GCG
A R N M E N I T S G F L G P L L V L Q A
GCG CTG AAC ATG GAG AAC ATC ACA TCA GGA TTC CTA GGA CCC CTG CTC GTG TTA CAG GCG

GGG TTT TTC TTG TTA ACA AGA ATC CTC ACA ATA CCG CAG AGT CTA GAC TCG TGG TGG ACT
G F L L T R I L T I P Q S L D S W W T
GGG TTT TTC TTG TTA ACA AGA ATC CTC ACA ATA CCG CAG AGT CTA GAC TCG TGG TGG ACT

TCT CTC AAT TTT CTA GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA AGC
S L N F L G G T T V C L G Q N S Q S P T
TCT CTC AAT TTT CTA GGG GGA ACT ACC GTG TGT CTT GGC CAA AAT TCG CAG TCC CCA AGC

TCC AAT CAG TCA CCA ACC TCC TGT CTT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTG
S N H S P T S C P P T C P G Y R W M C L
TCC AAT CAG TCA CCA ACC TCC TGT CTT CCA ACT TGT CCT GGT TAT CGC TGG ATG TGT CTG

CGG CGT TTT ATC ATC TTC CTC TTC ATC CTG CTG CTA TGC CTC ATC TTC TTG TTG GTT CTT
R R F I I F L F I L L L C L I F L L V L
CGG CGT TTT ATC ATC TTC CTC TTC ATC CTG CTG CTA TGC CTC ATC TTC TTG TTG GTT CTT

CTG GAC TAT CAA GGT ATG TTG CGC GTT TGT CCT CTA ATT CCA GGA TCI TCA ACC ACC AGC
L D Y Q G M L P V C P L I P G S S T S
CTG GAC TAT CAA GGT ATG TTG CGC GTT TGT CCT CTA ATT CCA GGA TCA TCA ACC ACC AGC

ACG GGA CCA TGC AGA GGC TGC AGC ACT CCT GCT CAA GGA ACC TCT ATG TAT CCC TCC TGT
T G P C R A C T P A Q G T S M Y P S C
ACG GGA CCG TGC AGG ACC TGC AGC ACT CCT GCT CAA GGA ACC TCT ATG TAT CCC TCC TGT
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FIG.4A

TGC TGT ACA AAA CCT TCG GAT GGA AAC TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT  
 C C T K P S D G N C T C I P I P S S W A  
 TGC TGT ACA AAA CCT TCG GAT GGA AAC TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT  
  
 TTC GGA AAA TTC CTA TGG GAG TGG GCC TCA GCC CGT TTC TCC TGG CTC AGT TTA CTA GTG  
 F G K F L W E W A S A R F S W L S L L V  
 TTC GGA AAA TTC CTA TGG GAG TGG GCC TCA GCC CGT TTC TCC TGG CTC AGT TTA CTA GTG  
  
 CCA TTT GTT CAG TGG TTC GTA GGG CTT TCC CCC ACT GTT TGG CTT TCA GTT ATA TGG ATG  
 P F V Q W F V G L S P T V W L S V I W M  
 CCA TTT GTT CAG TGG TTC GTA GGG CTT TCC CCC ACT GTT TGG CTT TCA GTT ATA TGG ATG  
  
 ATG TGG TAC TGG GGG CCA AGT CTG TAC AGC ATC TTG AGT CCC TTT TTA CCG CTG TTA CCA  
 M L Y W G P S L Y I I L S P F L P L P  
 ATG TGG TAT TGG GGG CCA AGT CTG TAC AGC ATC TTG AGT CCC TTT TTA CCG CTG TTA CCA  
 W  
 ATT TTC TTT TGT CTT TGG GTA TAC ATT TAA  
 I F F C L W V Y I  
 ATT TTC TTT TGT CTT TGG GTA TAC ATT TAA

FIG.4B

Nucleotide sequence 492 to 675 encoding the "a" determinant for the mutant HBV strain.

T<sub>492</sub>AT CAA GGT ATG TTG CCC GTT TGT CCT CTA ATT CCA GGA TCT TCA ACC ACC AGC  
ACG GGA CCA TGC AGA G<sub>561</sub>CC TGC ACG ACT CCT GCT CAA GGA ACC TCT ATG TAT CCC TCC TGT  
TGC TGT ACA AAA CCT TCG GAT GGA AAC TGC ACC TGT ATT CCC ATC CCA TCA TCC TGG GCT  
TTC GGA AAA<sub>675</sub>

FIG.5

Amino acid sequence of the "a" determinant for the mutant HBV strain:

Y<sub>100</sub>QGMLPVCPLI<sub>110</sub>PGSSTTSTGP<sub>120</sub>CRACTTPAQG<sub>130</sub>TSMYPSCCCT<sub>140</sub>  
KPSDGNCTCI<sub>150</sub>PIPSSWAFCK<sub>160</sub>

FIG.6